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THE VALUE OF ROUTINE BLOOD-PROTEIN DETERMINATIONS*

Report of Results in 320 Consecutive Cases

H. H. SHUMAN, M.D.,† AND HAROLD JEGHERS, M.D.‡

BOSTON

RECENT medical literature is replete with papers stressing the clinical importance of blood-protein determinations. Unfortunately the complexity of quantitative protein determinations has hindered the widespread use of this procedure.

Until recently the most widely used methods for blood-protein determinations included the macro- and micro-Kjeldahl, the colorimetric and the refractometric methods. These are complex procedures, relatively expensive as to equipment and to upkeep, and time-consuming even in the hands of experienced technicians. Both the clinician and the laboratory worker have long been in search of simpler methods. Several have been introduced and, though helpful, lacked quantitative accuracy.

The recently introduced Kagan[1, 2] method combined for the first time simplicity with the desired quantitative accuracy. This method is rapid, the apparatus is inexpensive and the technic can be readily mastered by any technician.

Kagan checked the accuracy of this method against the macro-Kjeldahl method and found the greatest deviation in 107 specimens to be 0.48 gm. per 100 cc., with a mean deviation of 0.16 gm. For clinical purposes such small deviations are irrelevant.

On the medical services of the Boston City Hospital it is customary to order blood-protein determinations only when specifically indicated, because the total number performed by the laboratory must necessarily be limited. The acquisition of a Kagan proteinometer by one of us (H. H. S.) suggested the idea of doing routine blood-protein determinations on a large series of consecutive admissions to the Fifth Medical Service. The present paper summarizes and discusses the results secured in 320 such cases.

METHOD AND PROCEDURE

The falling drop method for determination of specific gravity was first published by Barbour and Hamilton.[3] Moore and Van Slyke[4] later worked out the relation between plasma specific gravity and plasma protein content. Kagan, using this knowledge, devised a practical clinical test whereby the total protein of blood could be determined by noting the rate at which a drop of serum or plasma fell a measured distance through a mixture of synthetic methyl salicylate and heavy California mineral oil. The principle of this method is based on Stokes law and is described in Kagan's papers. A standardized apparatus for performing this test is now available commercially.§

The technic used in our study was as follows: the blood of 320 patients admitted to the Fifth Medical Service during April and May, 1939, was subjected to Kagan's test, the blood sample being collected at the same time as that for the routine Hinton test. Two cubic centimeters was placed in a small, dry test tube and centrifuged until the serum separated from the clot. The serum and proteinometer were allowed to remain at room temperature for ten minutes before using. Kagan's technic was followed. By means of a calibrated pipette 0.015 cc. (15 cu. mm.) of serum was introduced into the glass cylinder of the proteinometer, and the time required for the drop of serum to fall 10 cm. through the oil was measured to one-tenth of a second by means of a stopwatch. The protein value of the serum was obtained from a calibrated chart, due correction being made for the temperature of the oil. Most of the determinations required less than one minute for their completion, and all were made by one of us (H. H. S.). A dietary history, obtained by clinical clerks working on the service, was available in the majority

*From the South Department, Boston City Hospital, the Department of Medicine, Boston University School of Medicine, and the Fifth (Boston University) Medical Service, Boston City Hospital. This work was aided by a grant from the David Bradford Osgood Fund.

†Formerly, assistant physician, South Department, Boston City Hospital; physician, Burbank Hospital, Fitchburg, Massachusetts.

‡Assistant professor of medicine, Boston University School of Medicine; junior visiting physician, Boston City Hospital.

§The Kagan proteinometer was obtained from E. H. Sargent & Co., Chicago.

of these cases. In 20 cases, blood was also submitted to the hospital chemical laboratory for protein determination by the Kjeldahl method.

Six to 8 gm. per 100 cc. is the commonly accepted normal variation for the total protein value in man, with the albumin-globulin ratio varying from 1.5 to 2.5.[5] Variations from normal include: hypoproteinemia (a total protein less than 6 gm. per 100 cc.), hyperproteinemia (a total protein over 8 gm. per 100 cc.), changes in the albumin-globulin ratio and, rarely, the presence of abnormal (Bence-Jones) protein. A shifted albumin-globulin ratio commonly accompanies the first two. Changes in the fibrinogen value, while too small to influence grossly the total value, are nevertheless important because of their effect on the sedimentation rate. The latter is said to be a rough index of the blood-fibrinogen value.[6]

Hyperproteinemia

For many years hyperproteinemia was little understood and but rarely detected. A recent review[7] of the literature showed that not only does the presence of hyperproteinemia have considerable diagnostic value, but its pathologic physiology accounts for many phenomena otherwise hard to explain. These may include the following changes in the blood: rouleaux formation, increased sedimentation rate, spontaneous precipitation of proteins, blood-protein precipitation by Hayem's solution while performing a red-blood-cell count, discrepancy in acid-base equivalence, failure of clot to retract, rapid coagulation, possible changes in osmotic pressure, anticomplementary Wassermann reactions, changes in viscosity and variation in isoelectric point.

In practically every case on record, the protein increase was in the globulin fraction, usually accompanied by an absolute diminution of albumin and a marked reversal of the albumin-globulin ratio. In rare cases, Bence-Jones protein or fibrinogen constituted the protein increase. Although protein values over 8.0 gm. per 100 cc. are stressed here, the same significance could be attached to values as low as 6.5 gm., provided evidence was obtained for marked reversal of the albumin-globulin ratio.

Table 1. *Common and Rare Causes of Hyperproteinemia.**

COMMON CAUSES	RARE CAUSES
Dehydration	Metastatic bone lesions
Multiple myeloma (60%)	Malaria
Lymphogranuloma inguinale (75%)	Still's disease
Subacute bacterial endocarditis (50%)	Erythema induratum (Bazin)
Leprosy (80%)	Syndrome of Bing and Neel[21]
Kala-azar (40%)	Early portal cirrhosis
Schistosomiasis (50%)	Syphilis
Boeck's sarcoid	Leukemia
	Filariasis
	Osteopathia osteopriva
	Tuberculosis
	Rheumatoid arthritis
	Trypanosomiasis

*The percentage values (based on a survey of the literature) represent the frequency with which hyperproteinemia is found in certain diseases.

Diagnostically, the finding of hyperproteinemia should suggest one of the conditions listed in Table 1.

Hypoproteinemia

Hypoproteinemia is considered present when the total blood-protein level falls below 6 gm. per 100 cc. Most commonly one finds the decrease to be due to the lowering of the albumin fraction, accompanied or followed by a relative increase in globulin and a reversal of the albumin-globulin ratio. That edema may develop when the total protein falls below 5 gm. per 100 cc. has been well demonstrated,[8] but unfortunately application of this knowledge in clinical practice is often lacking.

Table 2. *Causes of Hypoproteinemia.**

- Malnutrition:
  - Dietary:
    - Endemic and sporadic
    - Associated with chronic infection, pellagra and beriberi
  - Poor absorption:
    - Idiopathic
    - Diarrhea
    - Intestinal fistulas, ileostomy and so forth
    - Neoplasm of gastrointestinal tract
  - Poor utilization (?)
- Kidney diseases (with albuminuria):
  - Nephroses, all types
  - Glomerular nephritis, chronic
  - Amyloid kidney
- Liver diseases:
  - Cirrhosis
  - Extensive neoplasm
- Protein dilution:
  - Excess fluid administration
  - Fever
  - Hyperthyroidism
- Protein loss:
  - Hemorrhage, acute or chronic
  - Weeping wounds or skin lesions
  - Shock, surgical and traumatic
- Heart failure
- Chronic poisoning:
  - Benzene, carbon tetrachloride, phosgene, phosphorus and so forth
- Toxemias of pregnancy

*Based on Kagan's classification.[22]

In the past, the effect of hypoproteinemia on the formation or aggravation of edema has been of interest chiefly to the internist.

Recent articles[9–11] suggest, however, that the significance of hypoproteinemia is greater than is generally believed. It may interfere with proper wound healing.[10] It may slow gastrointestinal peristalsis to a degree suggestive of intestinal obstruction, especially after a gastroenterotomy.[11] Since it thus increases the difficulties of gastrointestinal operations, it is of more than theoretical interest to the abdominal surgeon.

Hypoproteinemia is common in hyperthyroidism. That it may necessitate a two-stage procedure and have a suggestive relation to postopera-

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tive thyroid crisis brings the subject within the province of the thyroid surgeon.[12] The condition may be the responsible factor or at least aggravate certain types of toxemia of pregnancy, thus making the subject of interest to the obstetrician.[13] No doubt future studies will determine more fully the significance of hypoproteinemia.

The common causes of hypoproteinemia are given in Table 2. The complexities of this subject have been well reviewed by Melnick and Cowgill[14] and Moschcowitz,[15] and need no further comment here.

Results

A summary of the general results is shown in Table 3. In the group of 320 patients, 238 (74.5 per cent) had total protein determinations within the normal range of 6 to 8 gm. per 100 cc. Only 8 patients (3.3 per cent) had edema,* 6 of these presenting cases of cardiac decompensation.

Table 3. *Number and Percentage of Cases in Each Protein Range, with Number and Percentage Showing Edema.*

Protein Range	All Cases		Cases with Edema	
	No.	Per cent of total	No.	Per cent of group
gm. per 100 cc.				
Over 8.00	1	0.3	0	0
8.00–6.00	238	74.5	8	3
6.00–5.50	42	13.1	7	16
5.50–5.00	22	6.8	5	22
5.00 or less	17	5.3	7	41
Totals	320		27	

There were 42 patients (13.1 per cent) with total protein values ranging from 5.5 to 6.0 gm. per 100 cc., 7 of whom (16 per cent) had clinically recognizable edema.

Twenty-two patients (6.8 per cent) had total protein values in the range of 5.0 to 5.5 gm. per 100 cc., with 5 of them (22 per cent) showing edema. In only 1 case (a patient with avitaminosis) was there general anasarca. The diagnoses of patients in this group are given in Table 4, together with an estimate of the dietary intake of protein. In 4 cases the diet was considered to be adequate with regard to protein intake. Other mechanisms for producing hypoproteinemia in this group include poor absorption (cancer of colon), poor utilization (diabetes, acute and chronic infection) and heart failure.

Table 4. *Data from Cases with Blood-Protein Values of 5.00 to 5.50 Gm. per 100 Cc.*

Clinical Diagnosis	Blood Protein	Edema	Diet
	gm. per 100 cc.		
Diabetes mellitus	5.49	0	Inadequate
Tabes dorsalis	5.04	?*	?*
Lobar pneumonia	5.21	?	?
Pregnancy (7th month); bronchopneumonia	5.42	0	Adequate
Chronic sinusitis	5.49	0	?
Peripheral vascular disease	5.45	0	Adequate
Chronic alcoholism	5.35	+	Grossly inadequate
Lobar pneumonia	5.24	0	?
Mediastinal tumor	5.49	+++	?
Decompensated rheumatic heart disease	5.31	+++	?
Chronic alcoholism, beriberi	5.19	++++	Inadequate
Chronic alcoholism	5.40	0	Inadequate
Jacksonian epilepsy	5.35	0	Inadequate
Lobar pneumonia	5.31	0	?
Migraine	5.21	0	Adequate
Carcinoma of the colon	5.14	0	Inadequate
General avitaminosis	5.32	++++	Grossly inadequate
Duodenal ulcer	5.17	0	Inadequate
Acute tonsillitis	5.19	0	Inadequate
Pulmonary tuberculosis	5.35	0	Adequate
Chronic alcoholism	5.49	0	Inadequate
Bronchopneumonia	5.21	0	Inadequate

*Means that a specific statement was lacking in record.

Values of less than 5 gm. per 100 cc. were obtained for 17 patients (5.3 per cent). The relevant data are given in Table 5. The most significant finding was the presence of edema in 7 (41 per cent) of these patients, 4 of them showing marked edema of generalized distribution. Where available, the dietary history revealed a grossly inadequate protein intake in almost every case. Liver disease, infection, poor gastrointestinal absorption and utilization, loss of blood and heart disease were important additional factors producing hypoproteinemia in some of these cases. Two patients had clinically recognizable beriberi, 1 had the classical picture of scurvy, and 1 evidenced

Table 5. *Data from Cases with Blood-Protein Values below 5.00 Gm. per 100 Cc.*

Clinical Diagnosis	Blood Protein	Edema	Probable Reason for Hypoproteinemia
	gm. per 100 cc.		
Beriberi (polyneuritis), chronic alcoholism	4.90	++	Grossly inadequate diet
Portal cirrhosis, general avitaminosis	4.08	++++	Inadequate diet, liver disease
Chronic alcoholism, chronic bronchiectasis	4.90	0	Inadequate diet, chronic infection
Beriberi (polyneuritis), chronic alcoholism	4.83	++++	Grossly inadequate diet
Carcinoma of stomach	4.60	?	Anorexia, poor absorption
Advanced pulmonary tuberculosis	4.64	0	Chronic infection, anorexia
Psychogenic vomiting	4.87	0	Diet adequate but not retained
General avitaminosis, chronic alcoholism	4.73	0	Inadequate diet
Senility, bronchopneumonia	4.80	0	Infection, anorexia
Scurvy	4.83	++++	Grossly inadequate diet
Decompensated coronary heart disease	4.18	+++	Grossly inadequate diet
Decompensated rheumatic heart disease	4.55	+	Adequate diet (cause not determined)
Generalized arteriosclerosis, senility	4.97	0	Inadequate diet, anorexia
Carcinoma of large intestine	4.83	0	Inadequate diet, poor absorption
Bleeding peptic ulcer	4.69	0	Protein loss, poor diet
Idiopathic hypochromic anemia	4.93	++	Inadequate diet, poor absorption
Mucous colitis (7 years' duration)	4.93	0	Protein loss, poor absorption

*Edema here refers to peripheral pitting edema present on admission.

generalized vitamin deficiency. Less clear-cut evidence of deficiency — that is, dry or rough skin, stomatitis, glossitis, soft gums — was present in most of the other patients in this group, but such findings are naturally difficult to evaluate.

The large number of low protein values in our series suggested to us the necessity of checking the method in a group of healthy normal persons partaking of an adequate diet. Therefore, blood from 25 individuals (physicians, medical students, orderlies and technicians) was obtained and analyzed by the Kagan technic for total blood protein. The results are tabulated in Table 6. All,

TABLE 6. *Protein Values on Blood from 25 Normal Persons, Ages 24 to 35.*

BLOOD PROTEIN	NO. OF CASES
gm. per 100 cc.	
5.70–6.00	2
6.01–6.30	12
6.31–6.60	8
6.61–6.90	1
6.91–7.20	2

with 2 exceptions (5.93 and 5.70 mg. per 100 cc.) fell within the normal range. No adequate explanation for these two low values could be ascertained, the diet in each case being adequate. One could conclude that the low values for the hospital patients were not due to a tendency for this method to give low readings, but represent true cases of hypoproteinemia.

This is further shown to be true by comparing the 20 total blood-protein values obtained by the hospital chemical laboratory, where the standard

TABLE 7. *Comparison of Blood-Protein Values Obtained by the Falling-Drop Method with Those Obtained by Chemical Analysis.*

KAGAN FALLING-DROP METHOD	MACRO-KJELDAHL METHOD	MICRO-KJELDAHL METHOD	DEVIATION
gm. per 100 cc.	*gm. per 100 cc.*	*gm. per 100 cc.*	*gm. per 100 cc.*
6.18		6.3	+0.12
5.70		5.6	−0.10
6.11		6.4	+0.29
6.39		6.5	+0.11
5.63		5.9	+0.27
6.21		6.7	+0.49
6.18		6.0	−0.18
6.80	6.7		−0.10
5.90	6.0		+0.10
4.64	4.6		0.00
6.28	6.4		+0.12
6.00	6.0		0.00
5.97	6.1		+0.13
5.52	5.5		−0.01
5.49	5.4		0.00
6.14	6.1		0.00
6.97	6.5		0.47
6.69	6.7		+0.01
6.07	5.9		0.17
8.73	8.9		+0.17

macro- and micro-Kjeldahl methods are used, with those obtained by the Kagan technic. The figures are shown in Table 7. It can be seen that the greatest variation was 0.49 gm. per 100 cc., with an average deviation of 0.14 gm. Our results indicate clearly that the detailed chemical procedures are no more accurate for routine work than is the Kagan technic, and might well be dispensed with in any busy hospital laboratory.

In only 1 case was hyperproteinemia discovered, a value of 8.73 gm. per 100 cc. being obtained in a case of multiple myeloma. The formol-gel and Takata-Ara tests were strongly positive, which suggested, although the albumin-globulin ratio was not determined, that the globulin fraction was greatly increased. The main clue to the diagnosis in this case was the hyperproteinemia. Our results show that hyperproteinemia is considerably less common than hypoproteinemia, at least among the average run of medical cases seen in this district. On an active medical service one would be unlikely to find more than five or ten cases in the course of a year. The diagnostic significance of the condition is so great, however, that even the rare case is worthy of consideration.

It has been stressed that the protein level of 8 gm. per 100 cc. or over for the diagnosis of hyperproteinemia is only relative, for actually it is the presence of hyperglobinemia that is the more significant.[7] The Takata-Ara test is said to be positive when the globulin fraction is over 3 gm. per 100 cc.[16] and the formol-gel test usually positive when the globulin value reaches 4 gm.[17] For routine clinical work these simple laboratory procedures suffice to detect globulin increase and should be done along with the Kagan technic wherever possible. Only rarely will it be necessary to determine the globulin fraction by chemical analysis. Therefore, one should view any total protein of 7 gm. per 100 cc. or over with the same suspicion attached to values over 8 gm. per 100 cc., provided the albumin-globulin ratio proves to be reversed. It would perhaps be wisest to have every protein determination, regardless of its level, accompanied by some estimate of the globulin fraction.

COMMENT

It was a distinct surprise to find that almost 25 per cent of the patients in this series had a protein value below normal; 12.1 per cent of the determinations were less than 5.5 gm. per 100 cc., and 5.3 per cent were less than 5.0 gm. (the level commonly accepted as being clinically significant). Edema was distinctly commoner in the low-protein group, so much so, that in this hospital, at least, one would be justified in considering hypoproteinemia as the main, or at least a contributory, mechanism each time an edematous patient is studied. The difficulty of controlling cardiac decompensation in the presence of hypoproteinemia is particularly important,[18] and is probably

often overlooked. In other words, the presence of edema in any form indicates the necessity for determining the blood-protein level.

The influence of dehydration on the blood-protein level was not considered in our patients but is extremely important. It is common for very ill patients to be dehydrated on admission, thus increasing the total protein value of the blood. With restoration of the fluid to normal, subsequent determinations may show the blood protein to be diluted sufficiently to produce hypoproteinemia. Therefore, a true estimate of the blood-protein level cannot be secured until the fluid balance of the body has been restored to normal. This should be especially considered in those clinics where it is customary to take blood specimens immediately after the patient is admitted to the ward.

It is now generally accepted that few nutritional deficiencies occur singly. The discovery of one indicates the presence of others, even though not marked enough for clinical recognition. In this sense, the determination of the total blood-protein value is at present the easiest laboratory test available for detection of a dietary deficiency. The presence of hypoproteinemia indicates the need for a dietary history and a thorough search for the clinical minutiae suggestive of other deficiencies.

In our own series, abnormal protein values were found as commonly as significant deviations from normal in the routine urinalyses, blood nonprotein nitrogen and sugar determinations, blood counts, Hinton reactions and so forth.

In the past, technical difficulties discouraged follow-up studies on patients with abnormal protein values. This technic encourages such studies.

With regard to treatment, it is obvious that most persons with hypoproteinemia will respond favorably to dietary measures alone. However, the presence of liver disease and poor gastrointestinal absorption or utilization may preclude such a simple approach. Where necessary, intravenous therapy in the form of blood transfusion or, if available in the future for general human use, injections of lyophile serum[19] or aminoacids[20] would be indicated for temporarily increasing the blood-protein level. The latter methods have potentialities certain to stimulate further studies.

Summary

The blood-protein level for each of 320 medical patients and 25 controls was determined by the Kagan falling-drop technic. The method proved not only accurate but so simple that routine determinations were easily possible. Our results indicate that abnormal blood-protein values are commonly found on a general medical service. The significance of such changes has been briefly reviewed and discussed in the light of our results.

References

1. Kagan, B. M.: A simple method for the estimation of total protein content of plasma and serum. I. A falling-drop method for the determination of specific gravity. *J. Clin. Investigation* 17:369-372, 1938.
2. *Idem:* A simple method for the estimation of total protein content of plasma and serum. II. The estimation of total protein content of human plasma and serum by the use of the falling-drop method. *J. Clin. Investigation* 17:373-376, 1938.
3. Barbour, H. G., and Hamilton, W. F.: The falling-drop method for determining specific gravity. *J. Biol. Chem.* 69:625-640, 1926.
4. Moore, N. S., and Van Slyke, D. D.: The relationships between plasma specific gravity, plasma protein content and edema in nephritis. *J. Clin. Investigation* 8:337-355, 1930.
5. Cantarow, A., and Trumper, M.: *Clinical Biochemistry.* Second edition. 666 pp. Philadelphia: W. B. Saunders Co., 1939. P. 97.
6. Ham, T. H., and Curtiss, F. C.: Sedimentation rate of erythrocytes: influence of technical, erythrocyte and plasma factors and quantitative comparison of five commonly used sedimentation methods. *Medicine* 17:447-517, 1938.
7. Jeghers, H., and Selesnick, S.: Hyperproteinemia: its significance. *Internat. Clin.* 3:249-279, 1937.
8. Keefer, C. S.: Edema: Its pathologic physiology and clinical significance. *Internat. Clin.* 2:85-102, 1933.
9. Barden, R. P.; Thompson, W. D.; Ravdin, I. S., and Frank, I. L.: The influence of the serum protein on the motility of the small intestine. *Surg., Gynec. & Obst.* 66:819-821, 1938.
10. Thompson, W. D.; Ravdin, I. S., and Frank, I. L.: Effects of hypoproteinemia on wound disruption. *Arch. Surg.* 36:500-508, 1938.
11. Mecray, P. M., Jr.; Barden, R. P., and Ravdin, I. S.: Nutritional edema: its effect on the gastric emptying time before and after gastric operations. *Surgery* 1:53-64, 1937.
12. Bartels, E. C.: Serum-protein studies in hyperthyroidism. *New Eng. J. Med.* 218:289-294, 1938.
13. Strauss, M. B.: Observations on the etiology of the toxemias of pregnancy. V. The etiologic relationship between water retention and arterial hypertension. *Am. J. M. Sc.* 196:188-198, 1938.
14. Melnick, D., and Cowgill, G. R.: The problem of hypoproteinemia. *Yale J. Biol. & Med.* 10:49-63, 1937.
15. Moschcowitz, E.: Hypoproteinemia. *J. A. M. A.* 100:1086-1092, 1933.
16. Kirk, R. C.: The Takata-Ara test and its relation to cirrhosis of the liver. *J. A. M. A.* 107:1354-1357, 1936.
17. Wise, C. R., and Gutman, A. B.: The formol-gel reaction; a convenient preliminary test for hyperglobulinemia. *Am. J. M. Sc.* 194:263-270, 1937.
18. Ellis, L. B.: Plasma protein deficiency in patients with cardiac edema. *M. Clin. North America* 16:943-949, 1933.
19. Thompson, W. D.; Ravdin, I. S.; Rhoads, J. E., and Frank, I. L.: Use of lyophile plasma in correction of hypoproteinemia and prevention of wound disruption. *Arch. Surg.* 36:509-518, 1938.
20. Elman, R., and Weiner, D. O.: Intravenous alimentation, with special reference to protein (amino acid) metabolism. *J. A. M. A.* 112:796-802, 1939.
21. Bing, J., and Neel, A. V.: Two cases of hyperglobulinaemia with affection of the central nervous system on toxi-infectious basis. *Acta. Med. Scandinav.* 88:492-506, 1936.
22. Kagan, B. M.: personal communication.

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535 North Dearborn Street,
Chicago, Illinois.

REPORT OF MEETING

SUFFOLK DISTRICT MEDICAL SOCIETY

A regular meeting of the Suffolk District Medical Society was held at the Boston Medical Library on November 29, with Dr. Reginald Fitz presiding. Drs. William Leifer, Louis Chargin and Harold T. Hyman, of New York City, spoke on "The Theory and Practice of Massive Dose Chemotherapy by the Intravenous Drip Method in the Treatment of Syphilis." In introduction, Dr. Hyman discussed the history of intravenous therapy in general, with particular reference to experiments which showed that many untoward reactions were the result of "speed shock" which stimulated nitritoid crises and anaphylactoid reactions. Due credit was given Dr. Rudolph Matas, of New Orleans, who first used the intravenous route of therapy in 1888.

Dr. Hyman went on to tell of the conditions of their clinical experiments with the intravenous method of treating syphilis by massive chemotherapy. All cases were studied by a special committee, and no patients were seen by the original group after the termination of the primary phase of the treatment. A six-bed ward was provided at Mt. Sinai Hospital where the early cases were confined for one week. Follow-up visits were made to specified clinics, for which one dollar was paid for each visit as an inducement. Triplicate blood specimens were collected for examination by recognized independent serologists. Upon return to the clinic, there was a complete physical examination, but no treatment was given to any case.

Dr. Leifer then discussed the technical details of the intravenous chemotherapy which was employed. Without any specific preparatory treatment, the patients entered the hospital, where they were immediately put to bed. A 20-gauge needle was used, and the injection was always made into a vein of the mid-forearm, so that a minimal amount of immobilization was necessary. After an initial infusion of 20 or 30 cc. of 5 per cent glucose solution, 0.1 gm. of arsphenamine in about 125 cc. of the same solution was allowed to run into the vein in about one hour. At this rate for ten hours on four successive days, an average dose of about 4 gm. was administered. The patients were allowed out of bed each evening unless there was some individual contraindication. The recipients were given the routine hospital diet and high-carbohydrate fluids were forced. Pretreatment studies consisted of a complete blood count, a platelet count, a determination of the nonprotein-nitrogen level, the urobilin content and a van den Bergh test. Measurements of the arsenic excretion showed that about 20 per cent was recovered in the urine and somewhat over 30 per cent in the stools. Studies on bilirubin excretion on 10 successive patients showed that 3 developed liver dysfunction. No patients showed any toxic or nitritoid reactions or local infiltration. However, 44 per cent developed a mild phlebitis, and 24 per cent moderate nausea and vomiting, usually with the "primary fever." A few had headache and diarrhea.

Two types of fever developed. The primary phase occurred about five to seven hours after the first injection and was accompanied by the above-mentioned symptoms. The phenomenon, which was similar to a Herxheimer reaction, was noted in 57 per cent of the patients, but the temperature always returned to normal the same evening or by the next morning at the latest. Continuation of treatment resulted in no exacerbations. The secondary fever, which usually appeared about the fifth day, had an incidence of 63 per cent, was accompanied by toxic cutaneous eruptions in some instances, and lasted from two to six days.

The dermatological reactions were usually noted on the sixth to the eighth day and were shown to be in no way benefited by 200 mg. of cevitamic acid daily. This toxicoderma, with an incidence of 52 per cent, was often accompanied by fever, headache and arthralgia. If previous antisyphilitic treatment had been given, its appearance was earlier.

Two patients showed clinical as well as laboratory evidence of jaundice, while a larger number showed evidence of subclinical jaundice in the form of an elevated icteric index and bile in the urine. This, however, compared favorably with the incidence of these conditions in the ordinary arsenical treatment of syphilis where 1 patient in 75 and 1 in 4 have clinical and subclinical jaundice, respectively.

A marked decrease of platelets occurred twice; but one patient had previously had thrombocytopenic purpura and was relieved by splenectomy, while the other had reacted similarly to other methods of arsenical therapy.

Daily urinalyses occasionally demonstrated a transient slight albuminuria which soon cleared. There were no significant casts, and the nonprotein-nitrogen level remained normal.

Probably the most significant toxic manifestation was

the polyneuritis which occurred in 32 per cent of the first group of patients and in 38 per cent of the second, despite the administration to the latter of presumably adequate amounts of thiamin chloride. The onset of symptoms was two to three weeks following discharge, and the mild symptoms and minimal signs persisted for three to six months. There was never any motor involvement, and only 4 of 86 patients were incapacitated during this period. All showed complete spontaneous recovery.

There was only one fatality, and the presence of a positive Pandy test was cited as probable evidence that a hemorrhagic encephalitis was the cause of death. Dr. Leifer added that there is the same mortality rate (1 per cent) in the usual forms of treatment and that the unfortunate result was probably due to an inherent specific sensitivity to the drug.

Dr. Chargin compared the results of their treatment with those of other types of antisyphilitic therapy. Satisfactory results were obtained in 89 per cent of 78 observed cases, as compared with the 80 per cent of favorable results in a typical series of continuously and alternately treated patients. There were no positive cerebrospinal-fluid findings in any case. The principal advantages of the method were its short duration and the small dosage of arsenicals necessary. It was even suggested that smaller total amounts of the drug might eventually be employed.

Dr. Hyman, in conclusion, enumerated the following advantages of the continuous intravenous method of treating syphilis: the patient is made non-infectious within forty-eight hours; 100 per cent of those starting the course of treatment finish; and the total arsenical dosage is small. He said that they believed that, with the exception of the polyneuritis, all the so-called toxic manifestations were merely evidence of sensitivity to the drug itself.

In opening the discussion, Dr. Nels A. Nelson lauded the method as a possible boon to the public-health management of syphilis but deplored the unfortunate publicity given it as a sure four-day cure for the disease, which he felt would bring unbearable pressure on the local physician to use the still experimental therapeutic procedure. He also desired to know the cost of such a procedure.

Dr. Hyman assured him that publicity was the last thing they desired. The cost of approximately $100 per patient was not considered a true criterion of the eventual cost since that included all experimental work.

The only criticism offered by Dr. William Boardman was that a follow-up of two or three years was not adequate, even in cases entirely asymptomatic and free of signs. The speakers granted that this was merely a preliminary report of a long-term experiment.

Dr. Austin Cheever was of the opinion that, as yet, the various reactions were too high to warrant the use of this method of therapy in a disease where 28 per cent of patients are cured without treatment and an equal number remain asymptomatic despite positive serological tests. The obvious answer by Dr. Chargin was that it is impossible to know who are to be the lucky ones.

In answer to a question from Dr. Marshall Crawford, Dr. Hyman replied that no correlation had been attempted with the work of Eagles, who showed that a relatively low concentration of arsenicals inactivated the *Treponema pallidum* in vitro. It was believed that too many additional factors play a role in vivo to make these results applicable in practical chemotherapy.

NOTICES

FAULKNER HOSPITAL

The monthly clinicopathological conference of the Faulkner Hospital will be held on Thursday, March 7, at 5:00 p.m. There will be a discussion of cases by Drs. James A. Halsted and Arthur R. Kimpton.

Physicians and medical students are cordially invited to attend.

UNITED STATES MARINE HOSPITAL

The staff meeting of the United States Marine Hospital, Chelsea, will be held at "The Hut," on Friday afternoon, March 1, at 4:00. Mr. John C. G. Loring will talk, his subject being "Neurotic Alcoholism."

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Ether Dome of the Massachusetts General Hospital, on Tuesday, February 27, at 5:00 p.m.

PROGRAM

The Passage of Thiocyanate and Glucose from the Blood Stream into the Joint Spaces. Dr. J. W. Zeller.

Analysis of the Acoustics of the Stethoscope. Dr. H. B. Sprague and Mr. Maurice Rappaport.

Comparative Studies of the Effects of 200-Kilovolt and 1000-Kilovolt Roentgen Rays: The biologic effects on bone marrow, growing epiphyses and skin. Dr. E. A. Gall.

JEWISH MEMORIAL HOSPITAL

A meeting of the staff of the Jewish Memorial Hospital will be held in the hospital auditorium, 45 Townsend Street, Roxbury, on Thursday evening, February 29, at 8:30.

Dr. Joseph H. Pratt will speak on the subject "Pancreatic Disease." There will be an open discussion followed by a collation.

The medical profession is cordially invited to attend.

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday, February 27, in the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance), at 8:15 p.m.

PROGRAM

Presentation of cases.

The Life History of Bone Grafts: Experimental and clinical observations. Dr. Ralph K. Ghormley, Mayo Clinic, Rochester, Minnesota.

Medical students and physicians are cordially invited to attend.

BOSTON DISPENSARY

A luncheon meeting of the clinical staff of the Boston Dispensary will be held on Tuesday, February 27, in the auditorium of the Joseph H. Pratt Diagnostic Hospital at 12 o'clock noon. The subject of the meeting will be "The New England Medical Center: Its origin, present activities and future plans" by Mr. Arthur G. Rotch.

This meeting will inaugurate a series of talks on the past, present and future of the New England Medical Cen-

ter and its component parts. Talks in the following months will be given by Dr. Charles C. Cabot and Mr. Frank E. Wing on the Boston Dispensary, Dr. Leonard J. Carmichael on the Tufts College Medical School, Dr. Elmer W. Barron on the Boston Floating Hospital and Dr. Joseph H. Pratt on the Pratt Diagnostic Hospital.

Luncheon will be served to non-members at 35 cents. All interested persons are cordially invited to attend.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, February 28, from 2 to 4 p.m. Drs. Lyman Richards and Soma Weiss will speak on "Sore Throat."

Physicians and students are cordially invited to attend.

PETER BENT BRIGHAM HOSPITAL

A research conference of the medical staff of the Peter Bent Brigham Hospital will be held in the amphitheater of the hospital on Tuesday, March 5, at 5:00 p.m.

PROGRAM

Blood and Urine Iodine in Diabetes Insipidus. Drs. H. H. Blotner and H. J. Perkin.

Further Observations on Dynamics of Circulation in Patent Ductus Arteriosus. Dr. E. C. Eppinger.

All interested persons are cordially invited to attend.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

There will be a meeting of the New England Society of Physical Medicine at 8:00 on Wednesday evening, February 28, at the Hotel Kenmore, Boston. An informal dinner will be held in the Empire Room at 6:30.

PROGRAM

Symposium on the Treatment of Arthritis.

1. Orthopedics. Dr. L. T. Swaim.
2. Diet and Hygiene for the Arthritic. Dr. J. P. Bill.
3. The Use and Abuse of Physical Agents. Dr. H. A. Osgood.

All members of the medical profession are cordially invited to attend.

EDWARD K. DUNHAM LECTURES

The Faculty of Medicine of Harvard University has announced that the following lectures will be given by Dr. S. Walter Ranson, professor of neurology and director of the Institute of Neurology, Northwestern University Medical School, Chicago, under the Edward K. Dunham Lectureship for the Promotion of the Medical Sciences:

Monday, March 4. The Hypothalamus and the Sympathetic Nervous System.

Wednesday, March 6. Hypothalamicohypophysial Relationships.

Friday, March 8. The Hypothalamus and Behavior.

These lectures are scheduled for 5:00 p.m. at the Harvard Medical School, Amphitheater, Building C.

NEW ENGLAND PATHOLOGICAL SOCIETY

The meeting scheduled for February 15 was not held because of the storm and has been rescheduled for Thursday, February 29, at 8:00 p.m. at the Tufts College Medical School, 416 Huntington Avenue, Boston.

PROGRAM

Pathological Observations in Simmonds' Disease. Dr. R. C. Wadsworth.

Immediate Wheal and Erythema Type Reactions to Simple Chemical Substances. Dr. John Jacobs.

Pathological Findings in Leukoerythroblastic Anemia. Dr. S. B. Thorson.

Primary Tumor of the Heart. Dr. Harold Wood.

The pathological demonstrations will be available at 7:00 p.m. There will be a short business meeting followed by a collation.

Physicians and students are cordially invited to attend.

NORFOLK DISTRICT MEDICAL SOCIETY

The regular meeting of the Norfolk District Medical Society will be held in the Hotel Somerset, Boston, Tuesday evening, February 27, at 8:30. Tel. KEN 2700.

PROGRAM

Business.

The Uses and Abuses of Sulfanilamide and Related Compounds. Dr. Chester S. Keefer. Discussion will be opened by Dr. John F. Casey.

Collation.

AMERICAN PHYSICIANS' ART ASSOCIATION

The American Physicians' Art Association, composed of over eight hundred physicians in the United States, Canada and Hawaii who follow some form of fine or applied art as an avocation, will hold its next annual art show at the Belmont-Plaza, New York City, June 10–14, during the annual session of the American Medical Association. All physicians, in active practice or retired, who have an art hobby, including photography, are cordially invited to participate in the New York exhibit.

A physician may join this association by mailing a check for one dollar to the treasurer, Dr. R. W. Burlingame, San Francisco County Hospital, San Francisco, California, briefly stating what art medium the applicant follows. For detailed information kindly write to the executive secretary, Dr. F. H. Redewill, 526 Flood Building, San Francisco, California.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, FEBRUARY 25

SUNDAY, FEBRUARY 25

4 p.m. Sterility (lecture for women only). Dr. Donald Macomber. Free public lecture. Harvard Medical School, amphitheater of Building D.

4 p.m. Surgery of the Blood Vessels and Extremities. Dr. E. Everett O'Neil. Illustrated, public, health lecture. Faulkner Hospital auditorium.

MONDAY, FEBRUARY 26

*8:15 p.m. New England Heart Association. Children's Hospital, Boston.

TUESDAY, FEBRUARY 27

*9–10 a.m. Suppurative Disease of the Lungs. Dr. L. F. Davenport. Joseph H. Pratt Diagnostic Hospital.

*12 m. The New England Medical Center: Its origin, present activities and future plans. Mr. Arthur G. Rotch. Boston Dispensary.

5 p.m. Hospital Research Council, Massachusetts General Hospital, Ether Dome.

*8:15 p.m. The Life History of Bone Grafts: Experimental and clinical observations. Dr. Ralph K. Ghormley. Harvard Medical Society, Peter Bent Brigham Hospital (Shattuck Street entrance).

8:30 p.m. The Uses and Abuses of Sulfanilamide and Related Compounds. Dr. Chester S. Keefer. Norfolk District Medical Society, Hotel Somerset, Boston.

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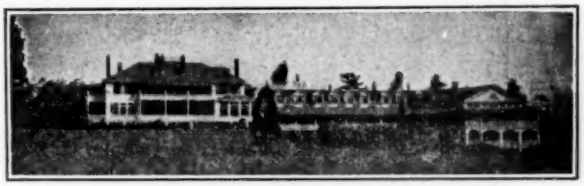

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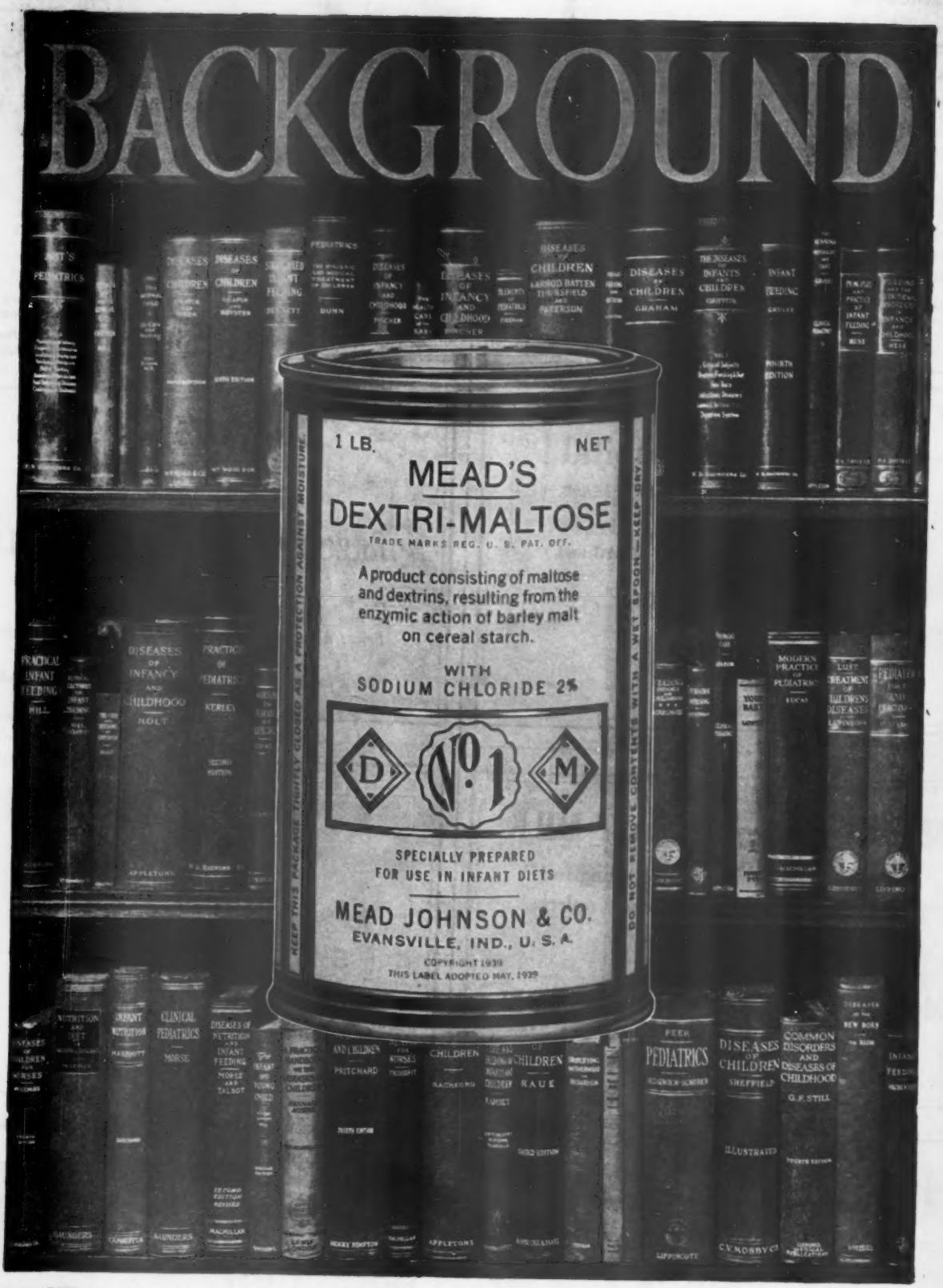
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